

Cutaneous Leishmaniasis Acquired in Jura, France

To the Editor: Cutaneous leishmaniasis is well established in the Mediterranean basin. However, the disease is spreading and new foci have been reported (1–3). Because of climate change, it is feasible that vector-borne diseases such as cutaneous leishmaniasis may spread northward into Europe (4). We report a patient who acquired cutaneous leishmaniasis while on holiday in Jura, France.

A previously healthy 49-year-old white man from the Netherlands traveled to France in August 2007. During August 2–17, he stayed at a camp site in Clairvaux-les-Lacs in a forested area near a lake. He made regular trips by foot in the surrounding area. Three months later, he noticed a swelling on his nose. In February 2008, he consulted a dermatologist who treated him twice with cryotherapy under a diagnosis of actinic keratosis, after which the lesion nearly disappeared.

Three months later, the patient again consulted the dermatologist when the lesion recurred. A biopsy result from the lesion was interpreted as an acute ulcerative inflammation without further specification. Treatment was continued with imiquimod 5% cream followed by erythromycin 2% cream with clobetasol 0.05% ointment. Because of a lack of improvement, this treatment regimen was alternated with tacrolimus 0.1% ointment until May 2008.

In November 2008, he consulted another dermatologist, who obtained a biopsy specimen in which a large number of intracellular microorganisms compatible with leishmaniasis were observed in histiocytes. The patient was then referred to the Department of

Dermatology at the Academic Medical Centre in Amsterdam. On examination, we found a plaque with a crusting surface and an erythematous border on the bridge of the nose (Figure, panel A). Regional lymph nodes were not palpable.

Revised histopathologic examination of the biopsy specimen showed a dermal inflammatory infiltrate of histiocytes containing numerous intracellular *Leishmania* amastigotes and epithelioid cells, lymphocytes, and few plasma cells (Figure, panel B). A direct smear from the biopsy specimen was positive for Leishman-Donovan bodies. Culture on Novy-MacNeal-Nicolle medium was positive for *Leishmania* spp. A PCR result for *Leishmania* performed on a biopsy specimen from the lesion was positive; sequence analysis showed DNA of *Leishmania donovani/infantum* complex.

Treatment was initiated with oral itraconazole (100 mg, 2×/d) for 6 weeks without improvement and was then continued with miltefosine (50 mg 3×/d) for 28 days. Other than nausea, the patient did not experience side effects. Regular monitoring of liver function showed values within normal limits. The lesion healed completely.

There are several reports of leishmaniasis acquired in Europe in locations north of the Mediterranean basin. Naucke et al. (5) reported 11 cases of endemically acquired leishmaniasis (human, canine, feline, and equine infections) in Germany since 1991. In 1992, a child with visceral leishmaniasis was described who had spent weekends and holidays near Calais, France (6).

We assume that our patient acquired cutaneous leishmaniasis in mainland Europe at 46°N. He had not visited leishmaniasis-endemic areas before this holiday in the French Jura.

Cutaneous leishmaniasis in France is found mainly in the region Pyrénées-Orientales, with 2 sandflies, *Phlebotomus ariasi* and *Phlebotomus perniciosus*, as vectors (7). One of the causative factors for the northward emergence of leishmaniasis in Europe is the spread of visceral and cutaneous leishmaniasis from disease-endemic areas in the Mediterranean to neighboring temperate areas with vectors without disease (8). A northward spread of leishmaniasis with an extension of the geographic range of *Ph. perniciosus* and *Ph. neglectus* sandflies has been found in Italy (9), and northward

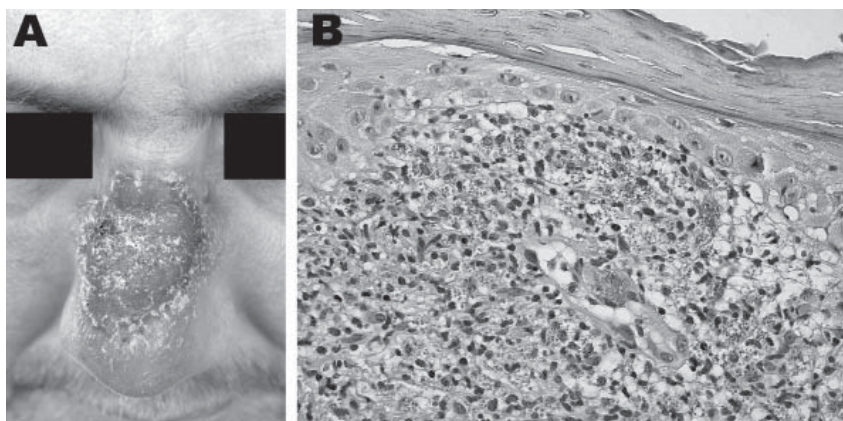


Figure. A) Crustous plaque on the nose of the patient. B) The epidermis shows parakeratosis, atrophy, and a single apoptotic keratinocyte. An inflammatory infiltrate is present in the papillary dermis, mainly composed of (epithelioid) histiocytes, admixed with lymphocytes and few plasma cells. B) Most macrophages in the infiltrate are parasitized by numerous *Leishmania* spp. amastigotes (hematoxylin and eosin stain, original magnification ×400). A color version of this figure is available online (www.cdc.gov/EID/article/18/01/11-0408-F1.htm).

spread of the proven sandfly vector *Ph. (Laroussius) perniciosus* and the competent sandfly vector *Ph. (Transphlebotomus) mascittii* into Germany (5). It has been hypothesized that sandflies have always been sporadically present in central Europe, but that climate change will lead to extended distribution (10).

It is tempting to assume that climate change resulted in cutaneous leishmaniasis at 46°N in France. In any event, our case and those reported by others should make clinicians aware of the possibility of cutaneous leishmaniasis outside the well-known disease-endemic areas.

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Visceral Leishmaniasis during Italian Renaissance, 1522–1562

To the Editor: Leishmaniasis, an infectious disease caused by parasites of the genus *Leishmania*, is transmitted to humans through the bite of a female sandfly. The 3 forms of leishmaniasis are visceral (VL) and cutaneous (CL), which are typical of the Old World, and mucocutaneous leishmaniasis, which occurs primarily in Central and South America. VL (also called kala-azar) is caused by species of the *L. donovani* complex (including *L. infantum*), and CL is mainly caused by *L. major* or *L. tropica* (1). In Italy,

VL and CL are caused by *L. infantum*. The origin and spread of leishmaniasis are a matter of debate. Widespread in antiquity, visceral leishmaniasis has been identified only in mummies from ancient Egypt and upper Nubia (2). Similarly, only 4 cases of mucocutaneous leishmaniasis have been identified in skulls from northern Chile (3).

We describe the identification of *L. infantum* infection in Eleonora from Toledo (1522–1562), wife of Cosimo I de' Medici and member of one of the major political Italian families during the Renaissance. The positive identification of *Leishmania* infection was achieved in bone samples by 2 independent approaches. First, a molecular ancient DNA (aDNA) analysis identified a specific 123-bp fragment of a conserved region of the minicircle molecule of the parasite's kinetoplast mitochondrial DNA (4,5) which on direct sequencing showed a *Leishmania*-specific sequence compatible with *L. infantum* (Figure; online Appendix Figure, wwwnc.cdc.gov/EID/article/18/1/10-2001-FA1.htm). This PCR result was independently replicated in 2 laboratories and additionally supported by the second approach, a protein assay showing a concomitant positive reaction by detecting IgG against *L. infantum* by Western blot sodium dodecyl sulfate–polyacrylamide gel electrophoresis.

Direct sequencing of the *Leishmania* aDNA identified a strain with high homology to *L. infantum*. Accordingly, we obtained a 98% concordance rate between our sequence and that of *L. infantum* (expect rate 6e-47, identity rate 113/118) (online Appendix Figure). The rates for other *Leishmania* species indicated that concordance for those species was less probable.

For the protein assay, fractionated proteins from a lysate of late-log-phase promastigotes of *L. infantum* ZMON-1 (World Health Organization